

## **REMARKS**

### **I. Status of the Application**

Claims 1-20 are pending in the application. Claims 1-20 were rejected.

5        Claims 4, 6-8, 13, and 15-17 were rejected as being indefinite.

Claims 1-18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Reiter, et al. (1976) Infection and Immunity 13:800-807 in view of Harrison's Principles of Internal Medicine.

10        Claims 8 and 17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Reiter, et al. (1976) Infection and Immunity 13:800-807 in view of Harrison's Principles of Internal Medicine and Stutman (1996) "The General Approach to Cystic-Fibrosis Related Pulmonary Infection in the United States" in Cystic Fibrosis Pulmonary Infections: Lessons from Around the World Birkhauser Verlag.

15        Claims 19 and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Reiter, et al. (1976) Infection and Immunity 13:800-807, in view of Harrison's Principles of Internal Medicine, and Ponikau (US Pat. 6,207,703).

Claims 10-18 are rejected on the ground of nonstatutory obviousness -type double patenting over parent US Pat. 6,702,998.

### 20    **II. The Amendments**

25        In the Specification, a typographical error in the author of the reference Cystic Fibrosis is corrected. Corrections from a misspelling and to format in reference to a trademark are made. On page 20, line 19, the Specification describes the combination of the claimed methods with "procedures used in the treatment of CF or other lung infections". Language for this is incorporated by reference into the Specification from references from page 1. This also provides support for claim language in some amended or newly added Claims.

30        In particular, the Merck Manual indicates that chest physical therapy including postural drainage, percussion, vibration, and assisted coughing is recommended. Hodson describes that airway clearance techniques (ACTs) are measures used at most stages of CF to improve microcilliary clearance; that chest physiotherapy using

percussion and postural drainage, as well as specialized breathing exercises, are utilized by patients worldwide; and discusses these in greater detail in Chapter 19. Bauernfeind describes use of chest percussion and postural drainage, airway vibration (using a flutter valve), positive expiratory pressure (PEP), and other forced expiratory techniques. And Harrison's describes that techniques for clearing pulmonary secretions include a combination of breathing exercises and chest percussion. These descriptions are briefly summarized in the added sentence to page 20.

Claim 2 is amended to alternatively also recite what was originally in Claim 3. Support also is recited, e.g., on page 4, lines 27-29. The hydrogen peroxide administration may be either direct or indirect.

Claim 4 is amended to delete an extraneous word, and the deleted language is the subject of newly added dependent Claim 21. Support is recited additionally, e.g., on page 4, lines 30-32.

Claim 6 is amended to delete an extraneous word.

Claim 7 is revised to list alternatives in text form, plus to add additional alternative embodiments recited in original Claim 8. The alternative embodiments are also recited, e.g., in text on page 4, line 35 to page 5, line 4.

Claim 8 is amended to clearly recite specific embodiments originally recited in the claim, and were further recited, e.g., on page 5, line 1 and page 11, line 33.

Claim 9 is amended to remove an extraneous word.

Claim 11 is amended to incorporate a limitation to a primate, which finds support, e.g., on page 17, lines 31-34. Specific embodiments are also incorporated from Claims 12 and 14, and are additionally recited, e.g., page 5, lines 11-12 and page 5, line 17.

Claim 18 is amended as the Examiner requested.

New Claim 21, as described, originated in Claim 4. New Claim 22 recites various alternative embodiments described, e.g., in original Claims 13, 15, and 17. These same alternatives were recited, e.g., on page 5, lines 14, 18, and 20-23. New Claim 23 continues in reciting particular exemplary embodiments described, e.g., in original Claims 14 and 16, and further recited on page 5, lines 12, 17, and 19. In particular, preventing progression of infection is included.

New Claim 24 originated in Claims 13 and 15. New Claim 25 originated in Claims 13 and 14. Text support is found, e.g., on page 5, lines 14-18.

New Claim 26 derives support, e.g., from page 5, lines 12-13, and page 9, lines 7-9.

5           New Claim 27 recites various alternative features for the inhaler, along the lines described earlier. In particular, the amount of hydrogen peroxide administered is effective to decrease microbial load, as described on page 19, lines 18-30. A request to correct a misspelling in Claim 20 was incorporated into new Claim 27. New Claim 28 expressly recites alternative embodiments of Claim 19.

10           No new matter is introduced by the claim amendments. Moreover, the new claim set numbers three independent claims, and 20 total claims. The application fee covers all necessary claim fees, so no additional fees should be needed.

### **The Rejections**

15   A. 112 Rejections

Claims 4, 6-8, 13, and 15-17 were rejected as being indefinite. In particular, any use of wording "including" has been deleted from the claims. Recitation of broad language in the Claims, e.g., to "lung condition," "enzyme," and airway clearance technique" are believed to be clear in the contexts used.

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B. 103 Rejections

The Examiner erroneously states on page 5 of the Office Action "This application currently names joint inventors ...." However, Applicant has been reminded of the continuing obligation to disclose relevant prior art during the pendency of proceedings.

25   As such, Applicants submit the appropriate 1449 forms listing known relevant art.

Claims 1-18 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Reiter, et al. (1976) Infection and Immunity 13:800-807 in view of Harrison's Principles of Internal Medicine.

30           Claims 8 and 17 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Reiter, et al. (1976) Infection and Immunity 13:800-807 in view of Harrison's Principles of Internal Medicine, and Stutman (1996) "The General Approach to Cystic-

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Claims 19 and 20 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Reiter, et al. (1976) Infection and Immunity 13:800-807, in view of Harrison's Principles of Internal Medicine, and Ponikau (US Pat. 6,207,703).

In each case, the rejections rely upon reports based on a lactoperoxidase enzyme found in milk fluids, and the observation that the intact system in milk fluids has a bactericidal activity. Further citation of the Bollen patent is used to extend the capacity of the intact milk fluid system to activity against viruses. The Harrison's reference is used to imply that using an intact milk fluid system known to possess bactericidal activity would be directly applicable in a very different body location with a reasonable expectation of success.

The Examiner apparently fails to recognize the distinction between the cited prior art and the claimed invention. On page 7, the Examiner states "Reiter lacks the teaching of using the LPThioHP system in a method of treating a lung condition associated with cystic fibrosis. This deficiency is cured by the teachings of Harrison's."

This suggests that the Examiner fails to appreciate that the invention claimed is further distinct from Reiter in that the claimed methods do NOT recite administering an intact LPThioHP system. The broadest claims do NOT require administration of an intact system, but only hydrogen peroxide, a substrate component of the intact system. No teaching or explanation is provided as to why administering a component fraction of a functional bactericidal system would provide a reasonable expectation of success to achieve the claimed result (treating infection in a lung) in a very different anatomical and physiological location.

Applicant believes the Examiner may view hydrogen peroxide as a recognized topical bactericide, and applies reasoning analogous to considering that a common product found on the drugstore shelf for treating topical bacterial infections would be both (1) obvious to try to apply to a respiratory tract AND (2) that that such treatment would be expected to be successful in such treatment. A substitute bactericide would be isopropanol, also found on drugstore shelves. In fact, there is reason to believe that isopropanol, at the concentrations found in the shelf product and even dilutions thereof,

would be highly detrimental to the respiratory system, e.g., by denaturing critical components therein. There are teachings AWAY from doing such. Similar considerations make the application of hydrogen peroxide (drugstore sources are in the 3% range, 3 grams per 100 ml), which corresponds to about 1 M (MW 34)) to the  
5 respiratory system inadvisable. As such, the required expectation of success does not exist for the use of hydrogen peroxide (or the hypothetical example isopropanol), but is based largely upon hindsight data provided by the teachings of the present application.

Applicant claims the administration of hydrogen peroxide, which is NOT an intact LPThioHP system. As such, the Reiter reference is not directly relevant to the claimed  
10 invention. Furthermore, it was not obvious that the mammalian lung is tolerant of adding some or all of the components of the LPThioHP system. It was not obvious that the lung could tolerate the addition of "an effective amount of hydrogen peroxide," nor that any effective amount would exist. A prima facie case for obviousness has not been made absent teachings of these, which are not provided by any combination of Bollen  
15 (antiviral activity), Stutman (CF lung clearance practices), or Ponikau (antifungal activity).

These factors teaching away apply in both the context of a primate exhibiting symptoms of cystic fibrosis (Claim 1) as well as the context of a mammal (Claim 10) or primate (Claim 11) suffering from a lung infection. In both cases, the ability of the lung  
20 to tolerate exogenous administration of the components is even less predictable.

The claimed methods provide the motivation for the inhaler device claims (Claims 19 and 27-28). Since the concept of administering the claimed substances into the lung were never suggested, the means for practicing these methods is novel and non-obvious.

25 As such, Applicant believes the rejections are improper and should be withdrawn.

C. Double Patenting

Claims 10-18 were rejected on the ground of nonstatutory obviousness -type double patenting over parent US Pat. 6,702,998. Applicant proposes to file a terminal disclaimer at a later date should allowable subject matter be recognized. Until then, such an action is unnecessary and premature. Should the Examiner deem that patentable subject matter exists herein, Applicant will submit an appropriate Terminal Disclaimer.

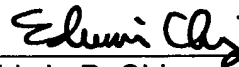
Conclusion

Applicant's current response is believed to be a complete response to all the outstanding issues of the latest Office Action. Further, the present response is a bona fide effort to place the application in condition for allowance. Accordingly, Applicant respectfully requests passage of the claims to allowance at the earliest possible convenience. Should the Examiner deem allowance inappropriate at this time, Applicant respectfully requests an interview be granted with the undersigned to discuss any issues.

Please continue to send all official written communications to the correspondence address in Florida.

Respectfully submitted,

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attached: proposed text of claims (Appendix A)

## Appendix A: Proposed Claims

1. A method of treating a lung condition in a primate exhibiting symptoms of cystic fibrosis, said method comprising administering to the respiratory system of said primate an effective amount of  $\text{H}_2\text{O}_2$ .
2. (amended) The method of Claim 1, wherein:
  - a) said administering is by inhalation of  $\text{H}_2\text{O}_2$ ; or
  - b) said administering is a formulation which produces  $\text{H}_2\text{O}_2$  in said respiratory system.
4. (amended) The method of Claim 1, wherein said lung condition comprises infection with:
  - a) bacteria;
  - b) fungus; or
  - c) virus.
5. The method of Claim 1, wherein said administering is in combination with:
  - a) administering a peroxidase; or
  - b) administering thiocyanate.
6. (amended) The method of Claim 1, wherein said administering is in combination with a treatment for a lung condition, a lung infection, or cystic fibrosis.
7. (amended) The method of Claim 6, wherein said treatment comprises:
  - a) administering an antibiotic, anti-fungal, or anti-viral;
  - b) administering a depolymerase; or
  - c) an airway clearance technique or physical therapy.
8. (amended) The method of Claim 7, wherein:
  - a) said depolymerase is a DNase; or
  - b) said treatment comprises one or more of a breathing exercise, postural drainage, chest percussion, vibration, or assisted coughing.
9. (amended) The method of Claim 1, wherein said  $\text{H}_2\text{O}_2$  is:
  - a) at a concentration between  $10^{-7}$  M and  $10^{-4}$  M in the lung fluid; or
  - b) administered between once in a week to hourly.
10. A method of treating a lung infection in a mammal, said method comprising administering to the respiratory system of said mammal an effective amount of  $\text{H}_2\text{O}_2$ .

11. (amended) The method of Claim 10, wherein said mammal is a primate and said administering is:

- a) by inhalation;
- b) a formulation which produces  $H_2O_2$  in said respiratory system; or
- c) in combination with a peroxidase or thiocyanate.

18. (amended) The method of Claim 10, wherein said  $H_2O_2$  is:

- a) at a concentration between  $10^{-7}$  M and  $10^{-4}$  M in the lung fluid; or
- b) administered between once a week to hourly.

19. An inhaler comprising:

- a) hydrogen peroxide;
- b) a peroxidase; or
- c) thiocyanate.

21. The method of Claim 4, wherein said bacteria comprises Staphylococcus aureus, Pseudomonas aeruginosa, or Burkholderia cepacia.

22. The method of Claim 11, wherein:

- a) said lung infection comprises bacteria;
- b) said administering is in combination with an additional treatment for cystic fibrosis;
- c) said administering is in combination with administering a depolymerase;
- d) said administering is in combination with an airway clearance technique or physical therapy; or
- e) said administering is in combination with at least one of a breathing exercise, postural drainage, chest percussion, vibration, or assisted coughing.

23. The method of Claim 11, wherein:

- a) said administering is in combination with administering thiocyanate;
- b) said administering is in combination with administering an antibiotic; or
- c) said treating prevents or decreases progression of said lung infection.

24. The method of Claim 10, wherein:

- a) said lung infection comprises bacteria, fungus, or virus; or
- b) said administering is in combination with an additional treatment for a lung condition, lung infection, or cystic fibrosis.

25. The method of Claim 24, wherein:

- a) said bacteria comprises Staphylococcus aureus, Pseudomonas aeruginosa, or Burkholderia cepacia; or
- b) said administering is in combination with thiocyanate.

26. The method of Claim 10, wherein said treating prevents or decreases progression of said lung infection.



27. The inhaler of Claim 19, which:
- a) administers an amount of hydrogen peroxide to the respiratory system of a mammal effective to decrease microbial load;
  - b) administers hydrogen peroxide in an amount between  $10^{-7}$  M and  $10^{-4}$  M in the lung fluid; or
  - c) further comprises an antibiotic, an anti-fungal, or an anti-viral.
28. The inhaler of Claim 19, comprising
- a) hydrogen peroxide;
  - b) thiocyanate; or
  - c) hydrogen peroxide and thiocyanate.